Assessment of Current Diagnostic Criteria for Guillain-Barré Syndrome

Arthur K. Asbury, MD,* and David R. Cornblath, MD†

Criteria for the diagnosis of Guillain-Barré syndrome are reaffirmed. Electrodiagnostic criteria are expanded and specific detail added.

Diagnostic criteria for Guillain-Barré syndrome (GBS) were devised in 1978 at the request of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS, now NINDS) [1]. The basis for issuing diagnostic criteria related to the swine flu vaccine incident of 1976–1977, which is reviewed in more detail elsewhere in the proceedings of this symposium [2]. At the previous conference on Guillain-Barré syndrome in 1981, clarification of these diagnostic criteria was offered (3). In the intervening eight years it has become apparent that further comments and elaboration on the diagnostic criteria first stated in 1978 are in order. The reader should recognize that the suggestions made below are solely the opinions of the authors and are not officially sanctioned by the NINDS or any neurological societies.

The definition of GBS and criteria for diagnosis are reproduced below as they were first published in the *Annals of Neurology* in 1978 [1]. These are followed by a series of comments and suggested modifications.

Definition of Guillain-Barré Syndrome and Criteria for Diagnosis

Guillain-Barré syndrome is a recognizable entity for which the basis for diagnosis is descriptive in our present state of knowledge. The features which allow a diagnosis include clinical, laboratory, and electrodiagnostic criteria. The problem is not with recognition of a typical case, but with knowing the boundaries by which the core disorder is delimited. The following criteria are established, in light of current knowledge and opinion, to define those limits.

The presence of preceding events is frequent, but they are not essential to the diagnosis. Most commonly, preceding events are viral infections, but the association of Guillain-Barré syndrome with preceding surgery, inoculations, and *Mycoplasma* infections is also known. In addition, Guillain-Barré syndrome occurs more frequently than by chance in the setting of preexisting illnesses such as Hodgkin's disease, lymphoma, or lupus erythematosus. Many patients with Guillain-Barré syndrome will have no history of any of these events, and the diagnosis should be made independent of them.

I. Features Required for Diagnosis

  A. Progressive motor weakness of more than one limb. The degree ranges from minimal weakness of the legs, with or without mild ataxia, to total paralysis of the muscles of all four extremities and the trunk, bulbar and facial paralysis, and external ophthalmoplegia.

  B. Areflexia (loss of tendon jerks). Universal areflexia is the rule, though distal areflexia with definite hyporeflexia of the biceps and knee jerks will suffice if other features are consistent.

II. Features Strongly Supportive of the Diagnosis

  A. Clinical features (ranked in order of importance)

   1. Progression. Symptoms and signs of motor weakness develop rapidly but cease to progress by four weeks into the illness. Approximately 50% will reach the nadir by two weeks, 80% by three weeks, and more than 90% by four weeks.

   2. Relative symmetry. Symmetry is seldom absolute, but usually, if one limb is affected, the opposite is as well.

   3. Mild sensory symptoms or signs.

   4. Cranial nerve involvement. Facial weakness occurs in approximately 50% and is frequently bilateral. Other cranial nerves may be involved, particularly those innervating the tongue and muscles of deglutition, and sometimes the extraocular motor nerves. On occasion (less than 5%), the neuropathy may begin in the nerves to the extraocular muscles or other cranial nerves.

   5. Recovery. It usually begins two to four weeks

From the *Department of Neurology, University of Pennsylvania School of Medicine, Philadelphia, PA, and the †Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD.

Address correspondence to Dr Asbury, Department of Neurology, Hospital of the University of Pennsylvania, 3400 Spruce St—3 West Gates Building, Philadelphia, PA 19104-4283.

after progression stops. Recovery may be delayed for months. Most patients recover functionally.

6. Autonomic dysfunction. Tachycardia and other arrhythmias, postural hypotension, hypertension, and vasomotor symptoms, when present, support the diagnosis. These findings may fluctuate. Care must be exercised to exclude other bases for these symptoms, such as pulmonary embolism.

7. Absence of fever at the onset of neuritic symptoms.

Variants (not ranked)

1. Fever at onset of neuritic symptoms.
2. Severe sensory loss with pain.
3. Progression beyond four weeks. Occasionally, a patient's disease will continue to progress for many weeks longer than four or the patient will have a minor relapse.
4. Cessation of progression without recovery or with major permanent residual deficit remaining.
5. Sphincter function. Usually the sphincters are not affected, but transient bladder paralysis may occur during the evolution of symptoms.
6. Central nervous system involvement. Ordinarily, Guillain-Barré syndrome is thought of as a disease of the peripheral nervous system. Evidence of central nervous system involvement is controversial. In occasional patients, such findings as severe ataxia interpretable as cerebellar in origin, dysarthria, extensor plantar responses, and ill-defined sensory levels are demonstrable, and these need not exclude the diagnosis if other features are typical.

B. Cerebrospinal fluid features strongly supportive of the diagnosis

1. CSF protein. After the first week of symptoms, CSF protein is elevated or has been shown to rise on serial lumbar punctures.
2. CSF cells. Counts of 10 or fewer mononuclear leukocytes/mm^3 in CSF.

Variants

1. No CSF protein rise in the period of one to ten weeks after the onset of symptoms (rare).
2. Counts of 11 to 50 mononuclear leukocytes/mm^3 in CSF.

C. Electrodiagnostic features strongly supportive of the diagnosis

Approximately 80% will have evidence of nerve conduction slowing or block at some point during the illness. Conduction velocity is usually less than 60% of normal, but the process is patchy and not all nerves are affected. Distal latencies may be increased to as much as three times normal. Use of F-wave responses often gives good indication of slowing over proximal portions of nerve trunks and roots. Up to 20% of patients will have normal conduction studies. Conduction studies may not become abnormal until several weeks into the illness.

III. *Features Casting Doubt on the Diagnosis*

1. Marked, persistent asymmetry of weakness.
2. Persistent bladder or bowel dysfunction.

3. Bladder or bowel dysfunction at onset.
4. More than 50 mononuclear leukocytes/mm^3 in CSF.
5. Presence of polymorphonuclear leukocytes in CSF.
6. Sharp sensory level.

IV. *Features That Rule Out the Diagnosis*

1. A current history of hexacarbon abuse (volatile solvents; *n*-hexane and methyl *n*-butyl ketone). This includes huffing of paint lacquer vapors or addictive glue sniffing.
2. Abnormal porphyrin metabolism indicating a diagnosis of acute intermittent porphyria. This would manifest as increased excretion of porphobilinogen and δ-aminolevulinic acid in the urine.
3. A history or finding of recent diphtheritic infection, either faucial or wound, with or without myocarditis.
4. Features clinically consistent with lead neuropathy (upper limb weakness with prominent wrist drop; may be asymmetrical) and evidence of lead intoxication.
5. The occurrence of a purely sensory syndrome.
6. A definite diagnosis of a condition such as poliomyelitis, botulism, hysterical paralysis, or toxic neuropathy (e.g., from nitrofurantoin, dapsone, or organophosphorus compounds), which occasionally may be confused with Guillain-Barré syndrome.

General Comment

Overall, the definition of GBS and criteria for diagnosis can be reaffirmed. Several aspects deserve further comment.

Two features are required for the diagnosis of GBS, progressive motor weakness and areflexia. Both of these requirements are qualified. Motor weakness must occur in more than one limb and, according to feature IIA2, relative symmetry on the two sides of the body is strongly supportive. Areflexia (loss of tendon reflexes) may be translated as some reflexes are lost, usually distally and symmetrically, and others are hypoactive, generally the more proximal ones. Also noteworthy is that weakness may precede attenuation of tendon jerks, usually by not more than two or three days, in the early phases of the illness.

Variant features as listed under IIA and IIB deserve comment. The term variant, as it is used here, refers to specific features that are on occasion seen in otherwise typical cases of GBS that run the expected course. The presence of one of these variant features does not rule out the diagnosis of GBS but should raise doubts. The presence of two variant features compounds suspicions that the diagnosis of GBS is incorrect.

In almost every instance of GBS, the malaise, fever, and respiratory or gastrointestinal symptoms of the preceding viral illness, if such occurred, have subsided by the time neuropathic symptoms appear. Therefore, manifestations of systemic illness (vomiting, abdominal pain, anemia, renal failure, eosinophilia) or constitutional symptoms (fever, anorexia, weight loss) or both,

either preceding or coinciding with evolution of neuropathy, strongly suggest a primary diagnosis of a systemic illness or intoxication with concomitant polyneuropathy, and not GBS. Possibilities include vaculitides, porphyrias, and acute intoxication with arsenic, lead, or disulfiram.

Cerebrospinal Fluid

In IIB, which deals with cerebrospinal fluid (CSF) findings in GBS, 10 or fewer mononuclear leukocytes per cubic millimeter is the expected finding, but 11 to 50 mononuclear leukocytes per cubic millimeter may on occasion be a variant feature. In the presence of human immunodeficiency virus (HIV) seropositivity, these limits require modification. In HIV seropositive patients with demyelinating neuropathy and a paucity of circulating CD4$^+$ T-cells, the mean CSF cell count was 23 cells/mm^3 on average as compared to a mean of fewer than 3 cells/mm^3 of CSF in HIV seronegative patients with GBS [4]. Thus in HIV seropositive patients the variant has become the norm for CSF pleocytosis.

Electrodiagnosis

Understanding of the electrophysiological features supporting the diagnosis of GBS has evolved considerably in the past ten years [5–10]. In the majority of GBS patients, electrodiagnostic studies reveal an evolving picture of multifocal demyelinating polyneuropathy with secondary axonal degeneration. Several corollaries to that statement are in order. First, normal or minimally abnormal studies may be obtained in 5 to 14% of individuals early in the course. Sequential studies will usually reveal a picture of a demyelinating neuropathy if that was not clear on the initial study. Second, the yield of findings consistent with demyelinating neuropathy is increased by the following: studying three or more motor nerves including late responses (F-waves and H-reflexes), evaluating proximal nerve segments, and performing precise enough measurements to determine whether partial conduction block and abnormal temporal dispersion exist.

The following discussion is limited to the results of nerve conduction studies performed in the first three weeks of illness, a time during which the majority of studies are performed for diagnostic purposes. In the first two weeks of GBS, the most common electrophysiological changes are partial conduction block, or decreased M-responses, or both. These occur in up to 75% of individuals. This figure contrasts with the lower percentage of abnormalities in conduction velocity apart from sites of "nerve entrapment" (20%), in distal latency (33%), and in temporal dispersion (20%). Evidence of conduction slowing is more common at usual sites of "entrapment" (60%): the median nerve at the wrist, the ulnar nerve in the across-elbow

segment, and the peroneal nerve in the across-fibular head segment. Abnormalities in late responses, either absent responses or prolonged responses, are also common, occurring in up to 46% of individuals studied in the first month, and reflecting the predilection of the disease for proximal nerve segments. Up to 90% of individuals will have abnormalities in some aspect of motor conduction studies in the first two weeks of illness. This figure rises to 96% by the third week of illness. Conversely, sensory conduction studies are abnormal in only 25% of individuals in the first week, rising to 73% of individuals by the third week. This is usually manifest as a reduction in evoked amplitude.

Electromyogram abnormalities are rare early in the course. Abnormal motor unit recruitment is the earliest change. Denervation potentials may occur in the second week but are more common after the third week.

The electrodiagnostic features of demyelination, listed below for convenience and discussed elsewhere in these proceedings [11], include reduced conduction velocity, conduction block, temporal dispersion, prolonged distal latencies, and prolonged or absent F-waves and H-reflexes. Occasional patients—fewer than 5%—show only evidence of axonal loss by physiological studies; these features of axonal loss include absent or severely reduced compound muscle action potential amplitudes evoked by nerve stimulation both near the muscle and at a distance; relatively preserved conduction velocities, to the extent that they can be measured; and later development of extensive muscle denervation [12, 13]. Whereas this pattern is known to occur in GBS, its occurrence raises the possibility of other diagnoses.

Proposed Electrodiagnostic Criteria for Demyelination of Peripheral Nerve

These criteria concern nerve conduction studies (including proximal nerve segments) in which the predominant process is demyelination.

Must have three of the following four features:

1. Reduction in conduction velocity in two or more motor nerves.
   a. <80% of lower limit of normal (LLN) if amplitude >80% of LLN.
   b. <70% of LLN if amplitude <80% of LLN.
2. Conduction block or abnormal temporal dispersion in one or more motor nerves: either peroneal nerve between ankle and below fibular head, median nerve between wrist and elbow, or ulnar nerve between wrist and below elbow.
   Criteria for partial conduction block:
   a. <15% change in duration between proximal and distal sites and >20% drop in negative-peak area of peak-to-peak amplitude between proximal and distal sites.

Criteria for abnormal temporal dispersion and possible conduction block:

- a. >15% change in duration between proximal and distal sites and >20% drop in negative-peak area or peak-to-peak amplitude between proximal and distal sites.

3. Prolonged distal latencies in two or more nerves.
   - a. >125% of upper limit or normal (ULN) if amplitude >80% of LLN.
   - b. >150% of ULN if amplitude <80% of LLN.

4. Absent F-waves or prolonged minimum F-wave latencies (10–15 trials) in two or more motor nerves.
   - a. >120% of ULN if amplitude >80% of LLN.
   - b. >150% of ULN if amplitude <80% of LLN.

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